REMARKS

Reconsideration of the patentability of applicants' claims is requested respectfully.

Status of the Claims

The Examiner's Action addresses all of applicants' pending claims, namely Claims 1, 3 to 39, 41, 42, 47, and 49 to 52. Claims 1, 13 to 16, 18 to 21, 24, 30, 37, 39, 41, 42, 47, 50, and 51 have been amended. Claims 2, 40, 43 to 46 and 48 were cancelled previously. New claims 53 to 66 have been added. Accordingly, there is presented for the Examiner's consideration Claims 1, 3 to 39, 41, 42, 47, and 49 to 66.

The addition of the phrase "said composition" to claims 1, 39, and 47, and of the phrase "said blend" to claim 41 makes clear that the subject drug and enhancer compositions are solid at room temperature as well as comprised of constituents which are solid at room temperature. The amendments are supported by the specification throughout and, in particular on page 15 at lines 9 to 11 which describe lubricants suitable for blending with "...the powder to be compressed ..." in reference to admixture compositions of the present invention comprising a drug, enhancer, and optional solid constituents from which tablets are prepared by direct compression.

The addition of the phrase "derivative of an acid" to claims 41 and 47 clarifies that all of the claimed functional groups are derived from a carboxylic acid functional group, as described in the specification on page 9, lines 10 to 16.

Editorial amendments or amendments defining particular embodiments of applicants' development have been made to claims 13 to 16, 18 to 21, 24, 30, 37, 39, 41, 42, 47, 50 and 51.

Added claims 53 to 66 define a solid oral dosage form which comprises a drug and, as the only enhancer present in the dosage form, a salt of a fatty acid which has a carbon chain length of from 6 to 20 carbon atoms (claim 53) or one of the "fatty acid" compounds which are referred to in claims 64 and 65, and claimed previously in claim 47. Support for this amendment is found at page 4, line 27 to page 5, line 16, and at page 8, line 25 to page 9, line 4, which describe a solid oral dosage form containing a drug and, as the only enhancer present in the dosage form, a fatty acid derivative compound. Additional support is found in the examples, for example: (a) Example 2, page 20, line 25 to page 21, line 5 which describes the preparation of tablet dosage forms containing a drug and a fatty acid sodium salt as the only enhancer present in the tablet; and (b) Example 5, page 27, line 21 to page 29, line 3, and Example 6, page 29, line 9 to page 30, line 24, each of which describe the preparation of a tablet dosage form containing heparin and, as the only enhancer present in the dosage form, sodium caprate, and, respectively, oral administration of these tablets to dogs and humans.

Summary of the Examiner's Rejections

In response to applicants' Request for Continued Prosecution and Preliminary Amendment filed December 16, 2002, the Examiner has reasserted the art rejections and arguments asserted in the Action of July 15, 2002 and cited for the second time in support thereof published international application WO 97/05903, inventors Watts *et al.* (hereafter, "the Watts reference").

Claims 1, 3-13, 15 to 39, 41, 42, and 49 to 52 have been rejected under 35 U.S.C. § 102 (b) as being anticipated by the Watts reference. Additionally, claims 1, 3 to 39, 41, 42, and 47 to 52 have been rejected under 35 U.S.C. § 103 (a) as being obvious over the

knowledge of one of ordinary skill in the art in view of the disclosure of the Watts reference.

Reconsideration of the Examiner's rejections is requested respectfully.

Summary of Applicants' Invention

Applicants have found surprisingly that, for a given concentration of an orally administered drug, the amount of a drug absorbed through membranes of the gastrointestinal tract can be increased (enhanced) to yield a therapeutically significant increase in serum level of the drug by administering orally a solid dosage form which contains the drug, and, as an enhancer, one or more of the fatty acid salts and/or derivatives that are defined in the claims of the present application (hereafter, for convenience, "applicants' fatty acid enhancer" - see, for example, claims 47 and 65 in which the enhancers are enumerated).

Applicants' claims define two basic embodiments of applicants' development. In one embodiment, the composition is defined as comprising room-temperature solids (hereafter "the all-solids composition" - see, for example, claims 1, 39, 41, and 47 and the claims depending therefrom). The other embodiment of applicants' development, the "fatty acid compound enhancer" embodiment, is defined as a dosage form in which the only enhancer present in the composition is one or more of applicants' fatty acid enhancers (see, for example, claims 53, 63, 66, and claims depending therefrom).

The all-solids composition of applicants' embodiment is prepared conveniently from an admixture of room-temperature solid constituents. Eliminating liquid or semi-solid constituents from the admixture avoids the need to place them into a solid form during preparation, for example, by encapsulation. Accordingly, applicants' development

has the benefits that equipment requirements and the number of unit operations for the preparation of the composition are reduced.

Applicants' claims which define the all-solids composition or the preparation thereof include independent claims 1, 41, 47, and 52.

Applicants' claims which define the "fatty acid compound enhancer" embodiment or the preparation thereof include independent claims 53, and 63 to 65.

The discussion which follows shows clearly that the reference of record neither anticipates nor renders obvious applicants' compositions or methods of preparing the compositions as defined in the claims. The disclosure of the reference cited by the Examiner in support of the rejections is summarized below.

Summary of the Disclosure of Published
International Application No. WO97/05903 (the Watts Reference)

The Watts reference discloses liquid or semi-solid compositions comprising a drug and an enhancer for enhancing transport of a polar drug through the membrane of the colon. The "Watts" enhancer comprises (page 5, lines 10-16):

(a) a mixture comprising members selected from the group consisting of fatty acids and fatty acid salts or a mixture comprising members selected from the group consisting of mono- and diglycerides of medium chain fatty acids; and

(b) a dispersing agent.

The Watts reference describes the dispersing agent as comprising one or more constituents which promote the dispersion of the composition within the colon (page 6, line 4). The dispersing agents which are exemplified in the Watts reference are liquid at room temperature, for example, polyglycolyzed glycerides and polyoxyethylene sorbitan fatty acid esters (page 6, line 26, to page 7, line 17). The Watts reference discloses also that fatty acids administered without a dispersing agent are not effective as enhancers of polar drug absorption (page 13, lines 24 to 28).

The Watts reference discloses that the subject drug/enhancer compositions are liquid or semi-solid, the precise state depending upon the constituents chosen (page 8, lines 21 to 23). The Watts reference discloses also that the semi-solid or liquid form of the drug/enhancer compositions described therein (page 8, line 21) is advantageous to the functionality of the composition, providing it with the ability to "...spontaneously emulsify in contact with aqueous media, (e.g. intestinal fluid)..." (see the Watts reference page 9 at lines 5 to 12).

The Watts reference describes also preparing a solid oral dosage form by encapsulating the semi-solid or liquid drug/enhancer composition in gelatin capsules. Additionally, the Watts reference discloses that the liquid or semi-solid compositions described therein may be encapsulated within "microcapsules", rendering it suitable for incorporation into a tablet or pellet dosage form using known techniques (page 9, lines 16-17).

Each of the examples of the Watts reference, consistent with Watts' general description of his development, discloses the preparation of a liquid composition comprising a drug, a fatty acid, and a liquid dispersing agent. Furthermore, consistent with the general description of his development, comparative Example 3 of the Watts reference discloses the preparation of a composition comprising a drug and a liquid fatty acid which fails to provide enhanced penetration of the drug.

Discussion of the Examiner's §102 Rejection

The Examiner's §102 rejection based on the Watts reference is traversed respectfully.

In her Action, the Examiner invites applicants to address the Examiner's earlier remarks in her Action dated July 15, 2002 regarding the Watts disclosure of the preparation of a tablet or pellet dosage form. In those earlier remarks, the Examiner asserted that applicants' claims which define room-temperature solid drug and enhancer constituents are not distinguished from the teaching of a tablet or pellet dosage form described in the Watts reference. In those remarks, the Examiner concurs with applicants that the Watts reference teaches only liquid or semi-solid drug and enhancer compositions.

In asserting her argument, the Examiner equates erroneously the physical form of a dosage form, for example, a tablet or a capsule (which is a solid dosage form) with the physical form(s) of the constituents that make up the dosage form and/or the physical form of the composition(s) that make up the solid dosage form. Watts discloses clearly that constituent(s) which make up the dosage form include liquid constituent(s) and that the composition which makes up the dosage form is a semi-solid or liquid composition. The Watts reference teaches clearly that the liquid or semi-solid compositions are micro-encapsulated prior to incorporation into a tablet or pellet dosage form (see the Watts reference, page 9 at line 17).

Applicants' claims 1, 41, and 47 distinguish definitively over the disclosure of the Watts reference in defining a composition in which all of the constituents from which the composition is formed are solids at room temperature and the composition which makes up the dosage form is a solid composition.

In summary, the Watts reference does not disclose such an "all-solids" composition. Accordingly, it does not anticipate independent claims 1, 41, and 47.

Added claims 53 to 66 define a dosage form containing a drug and, as the only enhancer present in the dosage form, one or more of applicants' fatty acid enhancers. The Watts composition contains an enhancer comprising not only a fatty acid-based constituent, but, in addition, a dispersing agent which functions as an enhancer. Accordingly, applicants' claims 53 to 66 distinguish over disclosures of the Watts reference.

Withdrawal of the §102 rejection is requested respectfully.

Discussion of the Examiner's §103 Rejections

Applicants' traverse respectfully the Examiner's §103 rejection. The Examiner asserts that the Watts reference teaches a composition which comprises a drug and a fatty acid salt and that it is well known in the art to form such a composition into a tablet, capsule, or pellet dosage form which is subsequently coated with a rate-controlling polymer. There is, however, more to the Watts disclosure than that portrayed by the Examiner. And the additional disclosure of Watts would lead one skilled in the art directly away from developing the subject matter of applicants' claims.

With regard to applicants' "all-solids composition" embodiment, the Watts reference teaches a liquid or semi-solid composition comprising a drug and enhancer and that the liquid or semi-solid form of the composition is advantageous to enhancing drug absorption through a target membrane (colon). The Watts reference, therefore, teaches away from applicants' solid drug and enhancer composition which comprises a mixture in which each constituent is a solid at room temperature, as defined in independent claims 1, 39, 41, 47, and 52.

With regard to applicants' "fatty acid compound enhancer" embodiment, the Watts reference teaches drug and enhancer compositions in a solid oral dosage form in

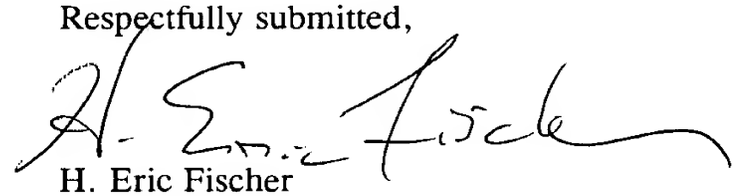
which the enhancer comprises at least two different types of constituents, a first constituent comprising one or more members selected from a broadly described generic group of fatty acid-based compounds and the other, as an essential constituent of the enhancer, a dispersing agent. The Watts reference teaches that a fatty acid-based constituent alone, for example, a fatty acid or a fatty acid salt, is ineffective to enhance drug adsorption (see the Watts reference page 13, lines 24 to 28). The Watts reference, therefore, teaches away from applicants' "fatty acid compound enhancer" composition which is defined in independent claims 53, and 63 to 65 as a dosage form which comprises, as the only enhancer present in the dosage form, one or more of applicants' fatty acid enhancers.

In view of the foregoing, applicants' request respectfully that the Examiner allow the application in an early and favorable Action.

It is requested respectfully that the Examiner telephone the undersigned if she believes a telephone interview would help to accelerate prosecution of the application.

This Reply is accompanied by a Petition for a one-month extension of the reply period, this is, from January 22, 2004 to February 22, 2004 (a Sunday).

Respectfully submitted,



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